Endogenous APOBEC3B restricts LINE-1 retrotransposition in transformed cells and human embryonic stem cells.

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Public Summary:
Members of the APOBEC3 (A3) family of cytidine deaminase enzymes act as host defense mechanisms limiting both infections by exogenous retroviruses and mobilization of endogenous retrotransposons. Previous studies revealed that the over-expression of some A3 proteins could restrict engineered human Long INterspersed Element-1 (LINE-1 or L1) retrotransposition in HeLa cells. However, whether endogenous A3 proteins play a role in restricting L1 retrotransposition remains largely unexplored. Here, we show that HeLa cells express endogenous A3B and A3C, whereas human embryonic stem cells (hESCs) express A3B, A3C, A3DE, A3F, and A3G. To study the relative contribution of endogenous A3 proteins in restricting L1 retrotransposition, we first generated small hairpin RNAs (shRNAs) to suppress endogenous A3 mRNA expression, and then assessed L1 mobility using a cell based L1 retrotransposition assay. We demonstrate that in both HeLa and hESCs, shRNA based knockdown of A3B promotes a ~2 to 3.7-fold increase in the retrotransposition efficiency of an engineered human L1. Knockdown of the other A3's produced no significant increase in L1 activity. Thus, A3B appears to restrict engineered L1 retrotransposition in a broad range of cell types, including pluripotent cells.

Scientific Abstract:
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